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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/892,206	06/26/2001	Thomas J. Brennan	R-171	9330

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DELTAGEN, INC.
1003 Hamilton Avenue
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EXAMINER	
BERTOGLIO, VALARIE E	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/892,206	BRENNAN ET AL.	
	Examin r	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,13-16 and 31-42* is/are pending in the application.

4a) Of the above claim(s) *1-4,13-16 and 31-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

2DETAILED ACTION

Applicant's amendment filed on 08/13/2003 has been entered. Claims 5-12 and 17-30 have been canceled. Claims 34-42 have been added. Claims 1-4,13-16, and 31-42 are pending and claims 34-42 are under consideration in the instant action.

Election/Restrictions

Claims 1-4,13-16, and 31-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14.

Claim Rejections - 35 USC § 101/112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly added claims 34-42 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well established utility.

The claims are directed to a transgenic mouse whose genome comprises a disruption in the endogenous mouse anaphylatoxin C3a receptor gene, and wherein the mouse exhibits relative to wild-type, reduced thymus weight, reduced thymus size, or reduced thymus to body weight ratio. The claims are further directed to cells and tissues isolated from the same mouse.

The instant specification teaches that the nucleotide sequence set forth in SEQ ID NO: 1 encodes the mouse anaphylatoxin C3a receptor. The instant specification has purported that mice whose genome comprises a disruption in the anaphylatoxin C3a receptor gene may be used to identify agents that modulate or ameliorate a phenotype associated with a disruption in SEQ IN NO: 1; see the pages 19-21.

The instant specification has disclosed a transgenic mouse whose genome comprises a disruption in the anaphylatoxin C3a receptor gene set forth by SEQ ID NO: 1, wherein the mouse exhibits relative to wild-type, reduced thymus weight, reduced thymus size, or reduced thymus to body weight ratio, see pages 53-54. The instant specification fails to discuss that a phenotype of reduced thymus weight, reduced thymus size, or reduced thymus to body weight ratio correlates with any disease or disorder. The specification has provided general assertions that the claimed transgenic mice may be used to identify agents that affect a phenotype related to the mice.

As such, the asserted utility, for the transgenic mouse embraced by the claims, of screening agents that may affect a phenotype, specifically reduced thymus weight, reduced thymus size, reduced thymus to body weight ratio, of said mouse as provided by the instant specification and encompassed by the claims, does not appear to be credible. The asserted utility does not appear credible to the skilled artisan since the evidence of record has not provided any suggestion of a correlation between an anaphylatoxin C3a receptor gene, the above-described phenotypes, and any disease or disorder. Since the evidence of record has not provided a correlation between these phenotypes and any disease or disorder, the utility of identifying agents that affect said phenotypes is not apparent. The evidence of record has not provided any

other utilities for the transgenic mouse embraced by the claims that are specific, substantial, and credible.

The asserted utility of the transgenic mouse embraced by the claims is based on the expectation that disrupting the nucleotide sequence set forth in SEQ ID NO: 1 would result in a detectable phenotype in the mouse that correlates with a disease state. While it is known in the art that enlargement of the thymus coincides with the onset and severity of systemic lupus erythematosus (Ravirajan et al., 1996, Clinical and Experimental Immunology, Vol. 105, pages 306-312, specifically, page 306, col. 1, lines 3-5; page 308, col. 1, lines 5-10), and the thymus has a role in other autoimmune diseases such as myasthenia gravis (Levinson et al, 2003, Immunologic Research, Vol. 27, pp. 399-408), there is no evidence of record that correlates a reduced thymus weight, reduced thymus size, or reduced thymus to body weight ratio to a disease. Levinson et al discuss potential molecular roles of the thymus however does not teach that the thymus size is affected in myasthenia gravis or any other autoimmune disease.

Therefore, the reference suggests a need to provide independent evidence of an association of reduced thymus weight, reduced thymus size, or reduced thymus to body weight ratio with a disease or disorder because neither the specification nor any art of record provides evidence of the existence of a correlation between the above mentioned phenotypes and a disease or disorder, leaving the skilled artisan to speculate and investigate the uses of the transgenic mouse embraced by the claims. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the transgenic mouse embraced by the claims. In light of the above, the skilled artisan would not find the asserted utility of the transgenic mouse embraced by the claims to be credible.

Claims 34-42 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Upon overcoming the utility and enablement rejections set forth above, the following issues of enablement under 35 USC 112-1st paragraph must also be addressed.

1) The specification fails to enable disrupting any anaphylatoxin C3a receptor gene in a mouse other than that set forth by SEQ ID NO:1. The claims lack a modifier before the phrase "endogenous mouse anaphylatoxin C3a receptor gene" and therefore the breadth of the claims includes mouse anaphylatoxin C3a receptor genes other than that set forth by SEQ ID NO:1. The evidence of record teaches only one anaphylatoxin C3a receptor gene (refer to Tornetta et al, 19997, Journal of Immunology, Vol. 158, pages 5277-5282). The specification does not provide adequate guidance for determining any other anaphylatoxin C3a receptor gene or that other anaphylatoxin C3a genes have the same function as the anaphylatoxin C3a receptor gene disclosed. Inserting the word "the" prior to the phrase "endogenous mouse anaphylatoxin C3a receptor gene", would overcome this rejection.

2) The breadth of claims 38-42 is such that they encompass chimeric animals (genetic mosaics) wherein only a portion of the cells of the animal comprises the claimed genetic disruption. The specification teaches making transgenic animals whose genome comprises a homozygous disruption in the anaphylatoxin C3a receptor gene in all somatic and germ cells wherein the mice display reduced thymus weight, reduced thymus size, reduced thymus to body

weight ratio, increased susceptibility to seizure or a stimulus processing deficit. The specification does not teach a chimeric animal with any of these phenotypes. The method of making genetic mosaic animals is such that each resulting chimera is comprised of a different, unpredictable ratio of cells of various genotypes. This ratio cannot be predetermined. Furthermore, the spatial distribution of cells of each genotype cannot be predetermined. Therefore, the phenotype of chimeric animals is not only dependent upon the genotype of the cells (which is unpredictable as set forth by the state of the art outlined on pages 8-9 of the previous office action; for example see Leonard; Moens; Griffiths) but is also dependent upon the spatial distribution of the cells and their relative population size. Thus, the phenotype of the chimeric animals encompassed by the claims is highly unpredictable. It would require undue experimentation for one of skill in the art to determine how to overcome the unpredictability associated with making chimeric animals such that the proportion and population of cells harboring a genetic alteration could be controlled in such a way as to increase the predictability of the phenotype of the resulting chimeric animal. Replacing the term "comprising" in line 1 of claims 38 and 41 with the phrase "whose genome comprises" is suggested.

3) Claims 38-42 encompass transgenic mice comprising a heterozygous disruption in the endogenous mouse anaphylatoxin C3a receptor gene. As set forth in the previous office action (refer to Leonard and Griffiths), the phenotype of knockout mice is unpredictable. The specification disclosed phenotypes exhibited by some knockout mice that comprise a homozygous disruption in the anaphylatoxin C3a receptor gene (pages 53-54); however, the specification does not teach a phenotype for mice comprising a heterozygous disruption in the anaphylatoxin C3a receptor gene that differs from a wild-type mouse. The specification asserts

that the claimed mice can be used for drug testing (pages 19-20), however, the specification fails to describe any phenotype for the mouse that correlates with a disease. The skilled artisan would not know how to use a transgenic knockout mouse that lacks a phenotype, particularly because the instant specification has not provided uses for such. Given the unpredictable nature if a phenotype that results from disruption of a nucleotide sequence, it would have required undue experimentation for the skilled artisan to use the claimed heterozygous knockout mouse that lacks a phenotype.

Newly added claims 34-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement as applied to cancelled claims 5-12,17-29 and 33 for reasons of record as set forth on pages 5-6 of the previous office action mailed 02/13/2003.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The basis of the rejection that the specification fails to describe the broad genera of genes encompassed by the claims applies to the newly added claims 34-42. Applicant's arguments have been fully considered and are not found persuasive. Applicant argues that the newly added claims are drawn to a transgenic mouse whose genome comprises a disuption in "the"

endogenous mouse anaphylatoxin C3a receptor" (page 5, line 1), however claims 34, 38 and 41, "...disruption in endogenous mouse anaphylatoxin C3a receptor gene" and are therefore not limiting to the mouse anaphylatoxin C3a receptor gene described in the specification. Therefore, as stated on pages 5-6 of the previous office action, the claims can be read as being drawn to more than one mouse anaphylatoxin C3a receptor gene and the specification only describes one mouse anaphylatoxin C3a receptor gene.

In the instant case the mouse anaphylatoxin C3a receptor genes encompassed by the claims lack a written description. The specification fails to describe what DNA molecules fall into this genus and it was unknown as of Applicants' effective filing date that any of these DNA molecules would have the property of encoding a anaphylatoxin C3a receptor polypeptide having the same structural and functional properties as that encoded by SEQ ID NO:1. The claimed embodiments of anaphylatoxin C3a receptor genes encompassed within the genus lack a written description. There is no evidence on the record of a relationship between the structures of the nucleotide sequences coding for a mouse anaphylatoxin C3a receptor and the nucleotide sequence set forth by SEQ ID NO:1 that would provide any reliable information about the structure of DNA molecules within the genus. The claimed invention as a whole is not adequately described if the claims require essential or critical elements that are not adequately described in the specification and that is not conventional in the art as of applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor

had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641,1646 (1998).

With the exception of the sequence referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved until reduction to practice has occurred regardless of the complexity or simplicity of the method of isolation. The skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic acid molecules and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In view of the above considerations one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by any member of the genus of genes encoding anaphylatoxin C3a receptor. Therefore, only the anaphylatoxin C3a receptor gene encompassed by **SEQ ID NO:1**, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that "to fulfill the written

description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention".

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The previous rejections of claims 5-10 under 35 USC 103 are withdrawn.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is 703-305-5469. The examiner can normally be reached on Mon-Weds 6:00-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on 703-305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

PETER PARAS
PATENT EXAMINER

Valarie Bertoglio
Examiner
Art Unit 1632